EFFICACY AND SAFETY OF TOPICAL ALPROSTADIL CREAM (VITAROS®) IN HYPERTENSIVE, DIABETIC AND CARDIAC PATIENTS WITH MALE ERECTILE DYSFUNCTION (ED)

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Oral Presentation: Dr. Jacques Buvat

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Convenient Topical Delivery of Alprostadil Cream (Alprostadil + DDAIP, Vitaros®)

DDAIP is a novel penetration enhancer. It acts by loosening the tight junctions of the skin.

Dosing Instructions

Single Dose (0.1ml cream) Dispenser

To be dispensed to tip of penis in drop wise manner, not inserted.
Integrates two multicenter, randomized, double-blind, placebo controlled trials with identical parallel groups design conducted at 82 sites in the USA (MED-2000-004/005)

Overall population: n= 1732 men with ED, 23 to 87 years old, mean age: 60.7 y
Population of this analysis: Men with Hypertension (n= 783, mean age: 62.9 y), Diabetes:(n= 382, mean age= 59.4 y), Cardiopathy (n=503, mean age: 64.5 y)

### Primary Efficacy Endpoints
- Change from baseline in Erectile Function domain of IIEF
- Sexual Encounter Profile (SEP) Questions 2 and 3

### Secondary Efficacy Endpoint
- Global Assessment Question (GAQ)
Integrated Intent-To-Treat (ITT) Efficacy Analysis in Hypertensive, Diabetic and Cardiac Subpopulations (1)

International Index of Erectile Function – Erectile Function Domain (IIEF-EF)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>200 mcg</th>
<th>300 mcg</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive</td>
<td>-0.6</td>
<td>2.9</td>
<td>2.0</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Diabetic</td>
<td>-1.2</td>
<td>3.5</td>
<td>2.1</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Cardiac</td>
<td>-1.7</td>
<td>1.5</td>
<td>1.9</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Overall</td>
<td>-0.7</td>
<td>2.5</td>
<td>2.4</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Hypertensive: n=187/175/198, Diabetic: n=81/94/85, Cardiac: n=115/122/135, Overall: n=408/405/417

Percentage of patients with IIEF-EF score change ≥ 4 (clinically significant change)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>200 mcg</th>
<th>300 mcg</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive</td>
<td>17</td>
<td>41</td>
<td>34.0</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Diabetic</td>
<td>15</td>
<td>46</td>
<td>35</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac</td>
<td>14</td>
<td>38</td>
<td>36</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Overall</td>
<td>20</td>
<td>40</td>
<td>40</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

Hypertensive: n=187/175/198, Diabetic: n=81/94/85, Cardiac: n=115/122/135, Overall: n=408/405/417
Integrated Intent-To-Treat (ITT) Efficacy Analysis in Hypertensive, Diabetic and Cardiac Subpopulations (2)

**SEP-3: Ability to maintain erection to ejaculation**
- **Hypertensive**:
  - Placebo: 26%
  - 200 mcg: 41%
  - 300 mcg: 35%
  - p = 0.001
- **Diabetic**:
  - Placebo: 29%
  - 200 mcg: 46%
  - 300 mcg: 33%
  - p = 0.002
- **Cardiac**:
  - Placebo: 23%
  - 200 mcg: 36%
  - 300 mcg: 31%
  - p = 0.003
- **Overall**:
  - Placebo: 30%
  - 200 mcg: 42%
  - 300 mcg: 39%
  - p < 0.001

**GAQ: When using study medication, did you feel your erections being improved?**
- **Hypertensive**:
  - Placebo: 20%
  - 200 mcg: 47%
  - 300 mcg: 49%
  - p < 0.001
- **Diabetic**:
  - Placebo: 20%
  - 200 mcg: 45%
  - 300 mcg: 53%
  - p = 0.001
- **Cardiac**:
  - Placebo: 17%
  - 200 mcg: 48%
  - 300 mcg: 50%
  - p < 0.001
- **Overall**:
  - Placebo: 20%
  - 200 mcg: 47%
  - 300 mcg: 52%
  - p < 0.001
**VITAROS® Safety**

Patients with at least one drug-related adverse event, n (%)  
- Placebo n=434: 51(14)  
- 200 mcg n=430: 178(41)  
- 300 mcg n=434: 182(42)

Drug-related serious adverse events:  
- Placebo: 0  
- 200 mcg: 0  
- 300 mcg: 0

Patients withdrawn due to drug-related adverse events, n (%):  
- Placebo: 0(0)  
- 200 mcg: 14(3)  
- 300 mcg: 25(6)
Conclusions

• **VITAROS®** demonstrated **statistically significant efficacy** across a broad range of ED severities and co-morbidities

• **VITAROS®** presents an **excellent safety profile**
  - No serious side effects
  - Most adverse events were localized to the site of application but were mild, short in duration and well tolerated

• **VITAROS®** shows the potential for **treating difficult to treat ED patients** such as those with hypertension, diabetes, and/or cardiac comorbidity...

  … it may offer a **1st choice treatment option for ED patients** of these specific categories as it is the case for every ED patient.
Back-Up: Age Group Analysis

Percent of Patients with IIEF-EF Change ≥ 4

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Placebo</th>
<th>200 mcg</th>
<th>300 mcg</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-54</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>55-69</td>
<td>p&lt;0.001</td>
<td>p=0.003</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>≥70</td>
<td>p=0.0023</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
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Age Groups
- 20-54
- 55-69
- ≥70
Back-Up: Body Mass Index (BMI) Analysis
Percent of Patients with IIEF-EF Change ≥ 4

<table>
<thead>
<tr>
<th>Body Mass Index (BMI)</th>
<th>Placebo</th>
<th>200 mcg</th>
<th>300 mcg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30 kg/m²</td>
<td>p=0.002</td>
<td>p&lt;0.0001</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

p<0.0001 for all comparisons.